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Amendments to the Claims

This listing of claims will replace all prior versions, and listings of claims in the application.

Claims 1-85 (Canceled).

Claim 86 (Currently Amended).   A method for producing a recombinant antibody having increased Fc mediated cellular cytotoxicity, comprising:

(a)   providing a mammalian host cell that expresses a recombinant antibody comprising an IgG Fc region containing N-linked oligosaccharides;

(b)   glycoengineering said host cell so that said host cell has an altered level of activity of at least one glycoprotein-modifying glycosyltransferase;

(c)   culturing said glycoengineered host cell under conditions which permit the production of said recombinant antibody; and

(d)   isolating said recombinant antibody;

wherein said recombinant antibody has increased Fc-mediated cellular cytotoxicity compared to the corresponding antibody produced by the same host cell that has not been glycoengineered.

Claim 87 (Currently Amended).   A method for producing a recombinant antibody having increased Fc receptor binding affinity, comprising:

(a)   providing a mammalian host cell that expresses a recombinant antibody comprising an IgG Fc region containing N-linked oligosaccharides;

(b)   glycoengineering said host cell so that said host cell has an altered level of activity of at least one glycoprotein-modifying glycosyltransferase;

(c)   culturing said glycoengineered host cell under conditions which permit the production of said recombinant antibody; and

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(d)   isolating said recombinant antibody;

wherein said recombinant antibody has increased Fc receptor binding affinity compared

to the corresponding antibody produced by the same host cell that has not been

glycoengineered.

Claim 88 (Previously Presented).   A method according to claim 86 or claim

87, wherein said activity is increased.

Claim 89 (Previously Presented).   A method according to claim 86 or claim

87, wherein said activity is decreased.

Claim 90 (Previously Presented).   A method according to claim 86 or claim

87, wherein said at least one glycoprotein-modifying glycosyl transferase is selected

from the group consisting of: β(1,4)-N-acetylglucosaminyltransferase III, β(1,4)-N-

acetylglucosaminyltransferase V, β(1,4)- galactosyltransferase, α-mannosidase II, and

core α-1,6-fucosyltransferase.

Claim 91 (Previously Presented).   A method according to claim 90, wherein

said at least one glycoprotein-modifying glycosyl transferase is β(1,4)-N-

acetylglucosaminyltransferase III.

Claim 92 (Previously Presented).   A method according to claim 90, wherein

said at least one glycoprotein-modifying glycosyl transferase is β(1,4)-

galactosyltransferase.

Claim 93 (Previously Presented).   A method according to claim 90, wherein

said at least one glycoprotein-modifying glycosyl transferase is α-mannosidase II.

Claim 94 (Previously Presented).   A method according to claim 90, wherein

said at least one glycoprotein-modifying glycosyl transferase is core α-1,6-

fucosyltransferase.

Claim 95 (Previously Presented).   A method according to claim 90, wherein said at least one glycoprotein-modifying glycosyl transferase is β(1,4)-N-acetylglucosaminyltransferase III and α-mannosidase II.

Claim 96 (Previously Presented).   A method according to claim 90, wherein said at least one glycoprotein-modifying glycosyl transferase is β(1,4)-N-acetylglucosaminyltransferase III and α-mannosidase II and β(1,4)-galactosyltransferase.

Claim 97 (Previously Presented).   A method according to claim 90, wherein said activity is expression of said at least one glycoprotein-modifying glycosyl transferase.

Claim 98 (Previously Presented).   A method according to claim 91, wherein expression of said β(1,4)-N-acetylglucosaminyltransferase III is increased.

Claim 99 (Previously Presented).   A method according to claim 93, wherein expression of said α-mannosidase II is increased.

Claim 100 (Previously Presented).   A method according to claim 95, wherein expression of both said β(1,4)-N-acetylglucosaminyltransferase III and said α-mannosidase II is increased.

Claim 101 (Previously Presented).   A method according to claim 94, wherein the activity of said core α-1,6-fucosyltransferase is decreased.

Claim 102 (Previously Presented).   A method according to claim 86 or claim 87, wherein said glycoengineering comprises introducing into said host cell at least one polynucleotide encoding an exogenous glycoprotein-modifying glycosyl transferase.

Claim 103 (Previously Presented).   A method according to claim 102, wherein said exogenous glycoprotein-modifying glycosyl transferase is β(1,4)-N-acetylglucosaminyltransferase III.

Claim 104 (Previously Presented).   A method according to claim 102, wherein said exogenous glycoprotein-modifying glycosyl transferase is α-mannosidase II.

Claim 105 (Previously Presented).   A method according to claim 102, wherein said exogenous glycoprotein-modifying glycosyl transferase is β(1,4)-N-acetylglucosaminyltransferase III and α-mannosidase II.

Claim 106 (Currently Amended).   A method according to claim 86 or claim 87, wherein said host cell is selected from the group consisting of an engineered CHO cell, an engineered BHK cell, an engineered NS0 cell, and an engineered SP2/0 cell, an engineered yeast cell, and an engineered plant cell.

Claim 107 (Previously Presented).   A method according to claim 106, wherein said host cell is an engineered CHO cell.

Claim 108 (Previously Presented).   A method according to claim 86 or claim 87, wherein said recombinant antibody has an increased proportion of nonfucosylated oligosaccharides in the Fc region as a result of said glycoengineering compared to the corresponding antibody produced by the same host cell that has not been glycoengineered.

Claim 109 (Previously Presented).   A method according to claim 86 or claim 87, wherein the predominant N-linked oligosaccharide in the Fc region of the antibody produced by said glycoengineered host cell is nonfucosylated.

Claim 110 (Previously Presented).   A method according to claim 86 or claim 87, wherein said recombinant antibody is a chimeric antibody.

Claim 111 (Previously Presented).   A method according to claim 86 or claim 87, wherein said recombinant antibody is a humanized antibody.

Claim 112 (Previously Presented).   A method according to claim 86 or claim 87, wherein said recombinant antibody is an antibody fragment that contains a Fc region.

Claim 113 (Previously Presented).   A method according to claim 86 or claim 87, wherein said recombinant antibody is a fusion protein that includes a Fc region of an immunoglobulin.

Claim 114 (Previously Presented).   A method according to claim 86 or claim 87, wherein the predominant N-linked oligosaccharide in the Fc region of said antibody produced by said glycoengineered host cell is not a high-mannose structure.

Claim 115 (Previously Presented).   A method according to claim 86 or claim 87, wherein the Fc region containing N-linked oligosaccharides in said antibody further comprises an increased proportion of GlcNAc residues compared to the corresponding antibody produced by the same host cell that has not been glycoengineered.

Claim 116 (Previously Presented).   A method according to claim 86 or claim 87, wherein said antibody produced by said glycoengineered host cell has an increased proportion of GlcNAc residues in the Fc region relative to the proportion of fucose residues compared to the corresponding antibody produced by the same host cell that has not been glycoengineered, and wherein said antibody has increased Fc-mediated cellular cytotoxicity as a result of said glycoengineering.

Claim 117 (Previously Presented).   A method according to claim 116, wherein said GlcNAc residues are bisecting.

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Claim 118 (Previously Presented). A method according to claim 116, wherein said GlcNAc residues are bisecting and wherein said bisected oligosaccharides are of complex type.

Claim 119 (Previously Presented). A method according to claim 116, wherein said GlcNAc residues are bisecting and wherein said bisected oligosaccharides are of hybrid type.

Claim 120 (Previously Presented). A method according to claim 86 or claim 87, wherein said antibody is a therapeutic antibody.

Claim 121 (Previously Presented). A method according to claim 86 or claim 87, wherein said antibody selectively binds to an antigen expressed by a cancer cell.

Claim 122 (Previously Presented). A method according to claim 114, wherein said antibody is a monoclonal antibody.

Claim 123 (Previously Presented). A method according to claim 120, wherein said antibody is selected from the group consisting of: an anti-CD20 antibody, an anti-human neuroblastoma antibody, an anti-human renal cell carcinoma antibody, an anti-HER2 antibody, an anti-human colon, lung, and breast carcinoma antibody, an anti-human 17-1A antigen antibody, a humanized anti-human colorectal tumor antibody, an anti-human melanoma antibody, and an anti-human squamous-cell carcinoma antibody.

Claim 124 (Canceled).

Claim 125 (Previously Presented). A method according to claim 86 or claim 87, wherein the majority of the N-linked oligosaccharides in the Fc region of said antibody produced by said glycoengineered host cell are bisected.

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Claim 126 (Previously Presented).   A method according to claim 86 or claim 87, wherein the majority of the N-linked oligosaccharides in the Fc region of said antibody produced by said glycoengineered host cell are nonfucosylated.

Claim 127 (Previously Presented).   A method according to claim 86 or claim 87, wherein the majority of the N-linked oligosaccharides in said Fc region of said antibody produced by said glycoengineered host cell are bisected, nonfucosylated.

Claim 128 (Previously Presented).   A method according to claim 114, wherein said antibody is a therapeutic monoclonal antibody having a human Fc region and that selectively binds an antigen expressed by cancer cells, and wherein the majority of oligosaccharides in the Fc region of said antibody produced by said glycoengineered host cell are nonfucosylated.

Claim 129 (Previously Presented).   A method according to claim 86 or claim 87, wherein at least 45% of the oligosaccharides in the Fc region of said antibody produced by said glycoengineered host cell are complex structures.

Claim 130 (Previously Presented).   A method according to claim 86 or claim 87, wherein said recombinant antibody produced by said glycoengineered host cell exhibits at least an 80% increase in maximal ADCC activity compared to the same antibody produced by the same host cell under identical culture and purification conditions, but which has not been glycoengineered.

Claim 131 (Previously Presented).   A method according to claim 86 or 87, wherein said at least one glycoprotein-modifying glycosyl transferase is mammalian.

Claim 132 (Previously Presented).   A method according to claim 131, wherein said at least one glycoprotein-modifying glycosyl transferase is human.

Claim 133 (Previously Presented). A method for lysing a target cell, said method comprising contacting said target cell with an antibody prepared by the method of claim 86 or claim 87.

Claim 134 (Previously Presented). A method according to claim 133, wherein said recombinant antibody produced by said glycoengineered host cell has an increased proportion of nonfucosylated oligosaccharides in the Fc region compared to the corresponding antibody produced by the same host cell that has not been glycoengineered.

Claim 135 (Previously Presented). A method according to claim 133, wherein the predominant N-linked oligosaccharide in the Fc region of said antibody produced by said glycoengineered host cell is nonfucosylated.

Claim 136 (Previously Presented). A method according to claim 133, wherein said antibody is a chimeric antibody.

Claim 137 (Previously Presented). A method according to claim 133, wherein said antibody is a humanized antibody.

Claim 138 (Previously Presented). A method according to claim 133, wherein said antibody is an antibody fragment that contains a Fc region.

Claim 139 (Previously Presented). A method according to claim 133, wherein said antibody is a fusion protein that includes a Fc region of an immunoglobulin.

Claim 140 (Previously Presented). A method according to claim 133, wherein the predominant N-linked oligosaccharide in the Fc region of said antibody produced by said glycoengineered host cell is not a high-mannose structure.

Claim 141 (Previously Presented). A method according to claim 133, wherein the Fc region containing N-linked oligosaccharides of the antibody produced by said

glycoengineered host cell further comprises an increased proportion of GlcNAc residues compared to the corresponding antibody produced by the same host cell that has not been glycoengineered.

Claim 142 (Previously Presented).   A method according to claim 133, wherein said antibody produced by said glycoengineered host cell has an increased proportion of GlcNAc residues in the Fc region relative to the proportion of fucose residues compared to the corresponding antibody produced by the same host cell that has not been glycoengineered, and wherein said antibody has increased Fc-mediated cellular cytotoxicity as a result of said glycoengineering.

Claim 143 (Previously Presented).   A method according to claim 142, wherein said GlcNAc residues are bisecting.

Claim 144 (Previously Presented).   A method according to claim 142, wherein said GlcNAc residues are bisecting and wherein said bisected oligosaccharides are of complex type.

Claim 145 (Previously Presented).   A method according to claim 142, wherein said GlcNAc residues are bisecting and wherein said bisected oligosaccharides are of hybrid type.

Claim 146 (Previously Presented).   A method according to claim 133, wherein said antibody is a therapeutic antibody.

Claim 147 (Previously Presented).   A method according to claim 133, wherein said antibody selectively binds to an antigen expressed by cancer cells.

Claim 148 (Previously Presented).   A method according to claim 133, wherein said antibody is a monoclonal antibody.

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Claim 149 (Previously Presented). A method according to claim 133, wherein said antibody is selected from the group consisting of: an anti-CD20 antibody, an anti-human neuroblastoma antibody, an anti-human renal cell carcinoma antibody, an anti-HER2 antibody, an anti-human colon, lung, and breast carcinoma antibody, an anti-human 17-1A antigen antibody, a humanized anti-human colorectal tumor antibody, an anti-human melanoma antibody, and an anti-human squamous-cell carcinoma antibody.

Claim 150 (Canceled).

Claim 151 (Previously Presented). A method according to claim133, wherein the majority of the N-linked oligosaccharides in the Fc region of said antibody produced by said glycoengineered host cell are bisected.

Claim 152 (Previously Presented). A method according to claim 133, wherein the majority of the N-linked oligosaccharides in the Fc region of said antibody produced by said glycoengineered host cell are nonfucosylated.

Claim 153 (Previously Presented). A method according to claim 133, wherein the majority of the N-linked oligosaccharides in said Fc region of said antibody produced by said glycoengineered host cell are bisected, nonfucosylated.

Claim 154 (Previously Presented). A method according to claim 133, wherein said antibody produced by said glycoengineered host cell is a therapeutic monoclonal antibody having a human Fc region and that selectively binds an antigen expressed by cancer cells, and wherein the majority of oligosaccharides in the Fc region of said antibody are nonfucosylated.

Claim 155 (Previously Presented). A method according to claim 133, wherein at least 45% of the oligosaccharides in the Fc region of said antibody produced by said glycoengineered host cell are complex structures.

Claim 156 (Previously Presented).   A method according to claim 133, wherein said recombinant antibody produced by said glycoengineered host cell exhibits at least an 80% increase in maximal ADCC activity compared to the same antibody produced by the same host cell under identical culture and purification conditions, but which has not been glycoengineered.

Claim 157 (Previously Presented).   A method according to claim 157, wherein said at least one glycoprotein-modifying glycosyl transferase is mammalian.

Claim 158 (Previously Presented).   A method according to claim 127, wherein said at least one glycoprotein-modifying glycosyl transferase is human.

Claim 159 (Previously Presented).   A method according to claim 86 or claim 87, wherein said glycoengineering comprises genetically manipulating said host cell so that said host cell has an altered level of activity of at least one glycoprotein-modifying glycosyltransferase.

Claim 160 (Previously Presented).   A method according to claim 121, wherein said antigen is differentially expressed by said cancer cell.

Claim 161 (Previously Presented).   A method according to claim 133, wherein said target cell is a tumor cell.

Claim 162 (Previously Presented).   A method according to claim 161, wherein said antibody specifically binds an antigen differentially expressed on said target cell.

Claim 163 (New). A method according to claim 86 or 87, wherein said IgG Fc region containing N-linked oligosaccharides comprises an entire IgG Fc region.

Claim 164 (New). A method according to claim 86 or 87, wherein said IgG Fc region containing N-linked oligosaccharides comprises an IgG fragment.

Claim 165 (New) A method according to claim 164, wherein said IgG fragment comprises a CH2 domain.